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MACHINE-LEARNING ASSISTED PHENOTYPING: FROM FUNGAL MORPHOLOGY TO MODE OF ACTION HYPOTHESIS

Sarah Laroui ¹, Eric Debreuve ¹, Xavier Descombes ¹, François Villalba ², Florent Villiers ², Aurélie Vernay ²

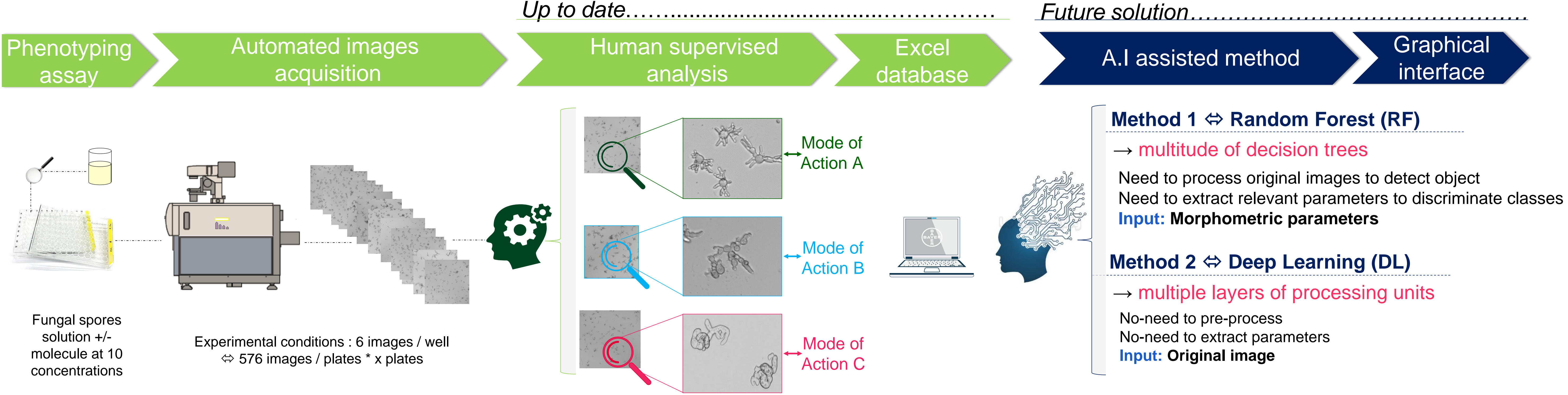
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Introduction

Beyond growth inhibition, fungicides can also trigger specific morphological modifications visualized under transmitted light microscopy. These morphological changes result from the activity of a given compound *via* the inhibition of a molecular target, commonly named as its mode of action (MoA). We are hence able to classify different molecules into their respective MoA by observing their phenotypic signature, and even to detect new MoA with unknown phenotypic effect for further deconvolution. The aim of the presented work is to develop a robust method for automated recognition and classification of these phenotypic signatures in order to lead to a Mode of Action hypothesis. We compare two machine-learning methods (Random forest and Convolutional Neural Network) for direct processing of images generated on the grey mold *Botrytis cinerea* subjected to different antifungal molecules.

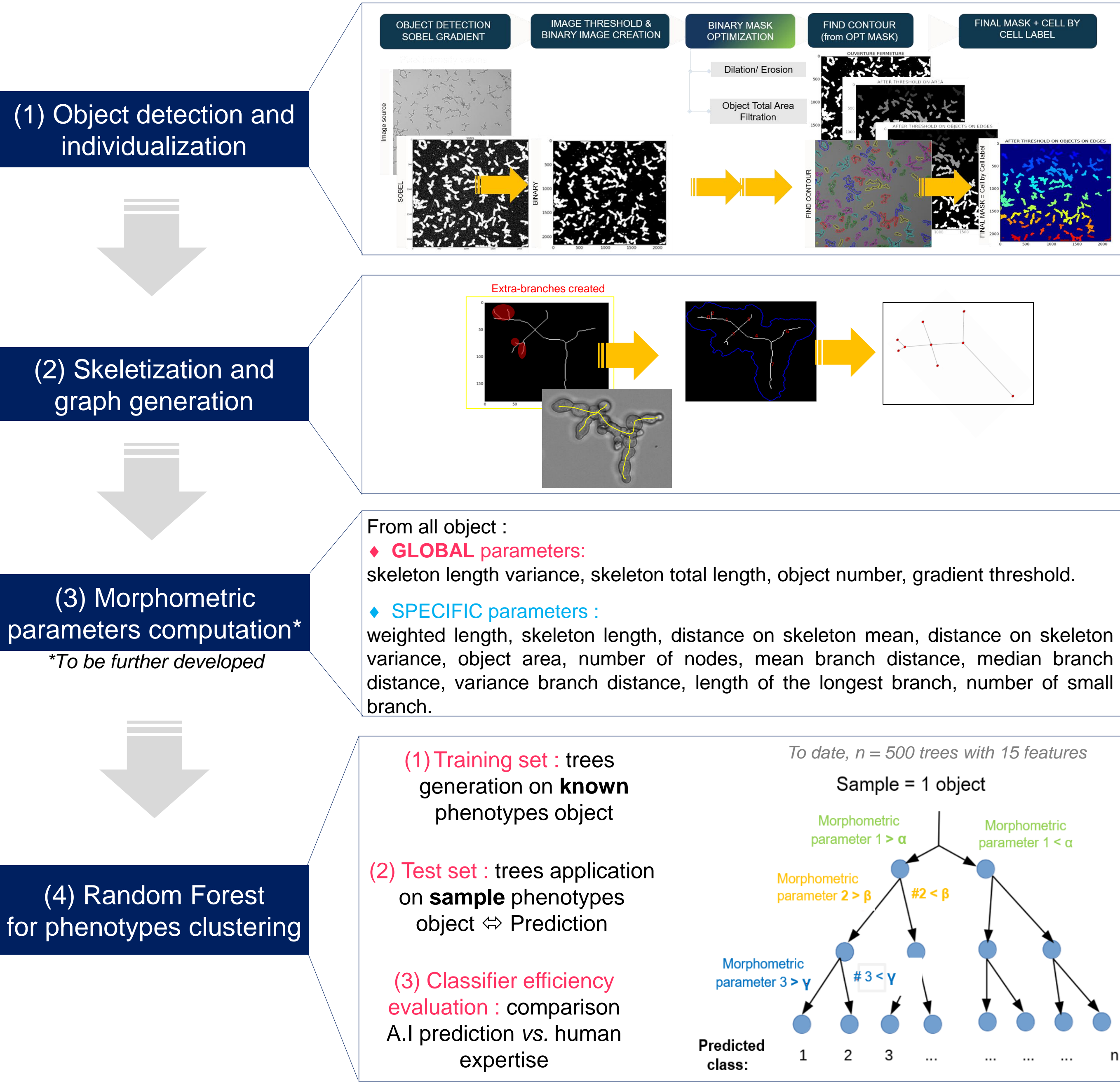
Strategy



From morphology recognition to Mode of Action prediction :
the power of artificial intelligence to automatize fungal precision phenotyping.

Method 1

Morphometric parameters extraction and Random Forest-based classification

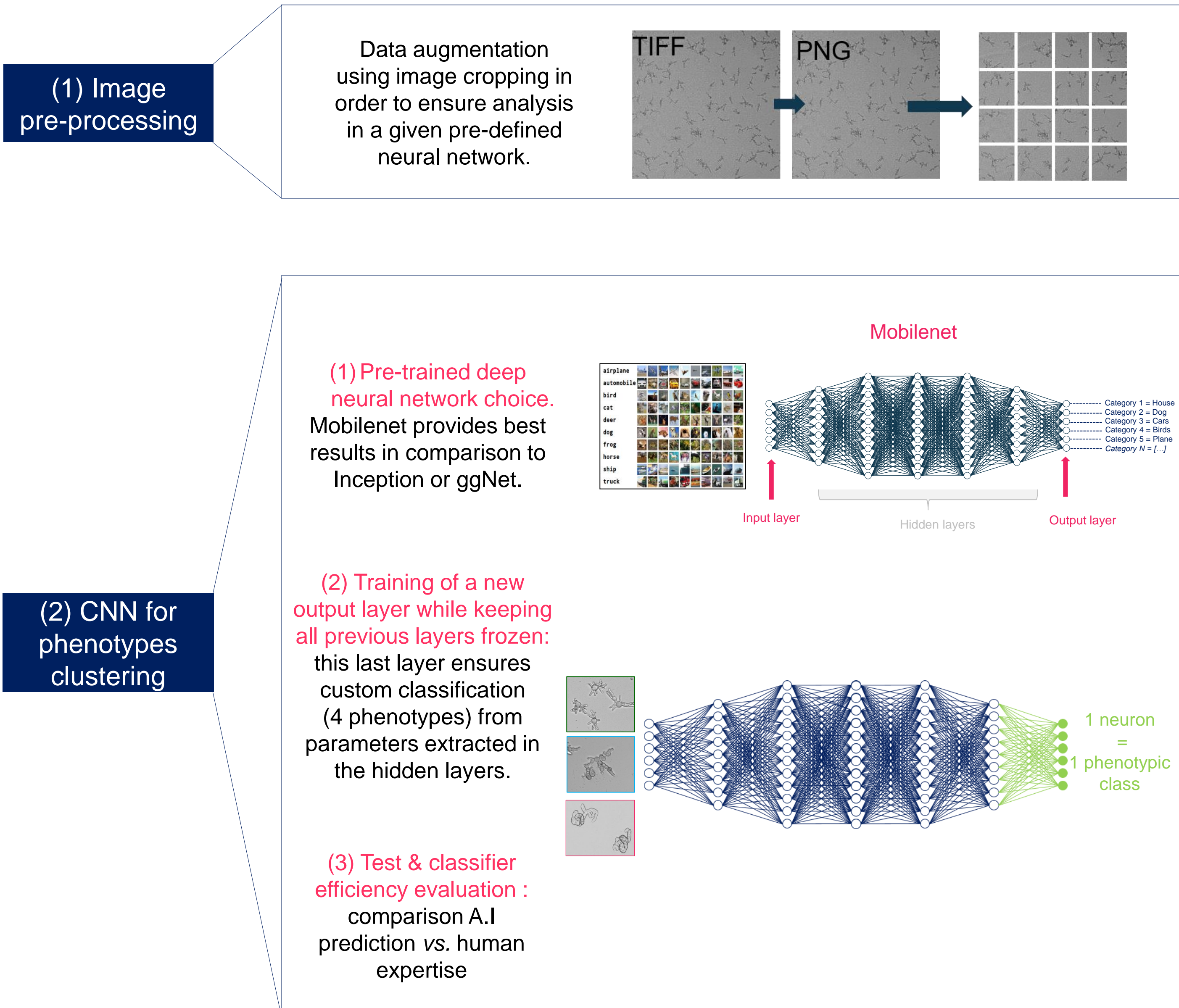


In summary :

Precise analysis and classification of cellular objects within images.
Access to known and defined morphometric features values.
Limited number of morphometric features.
Run time: few minutes / image

Method 2

Application of a pre-trained image recognition Convolutional Neural Network (CNN) for phenotype classification



In summary :

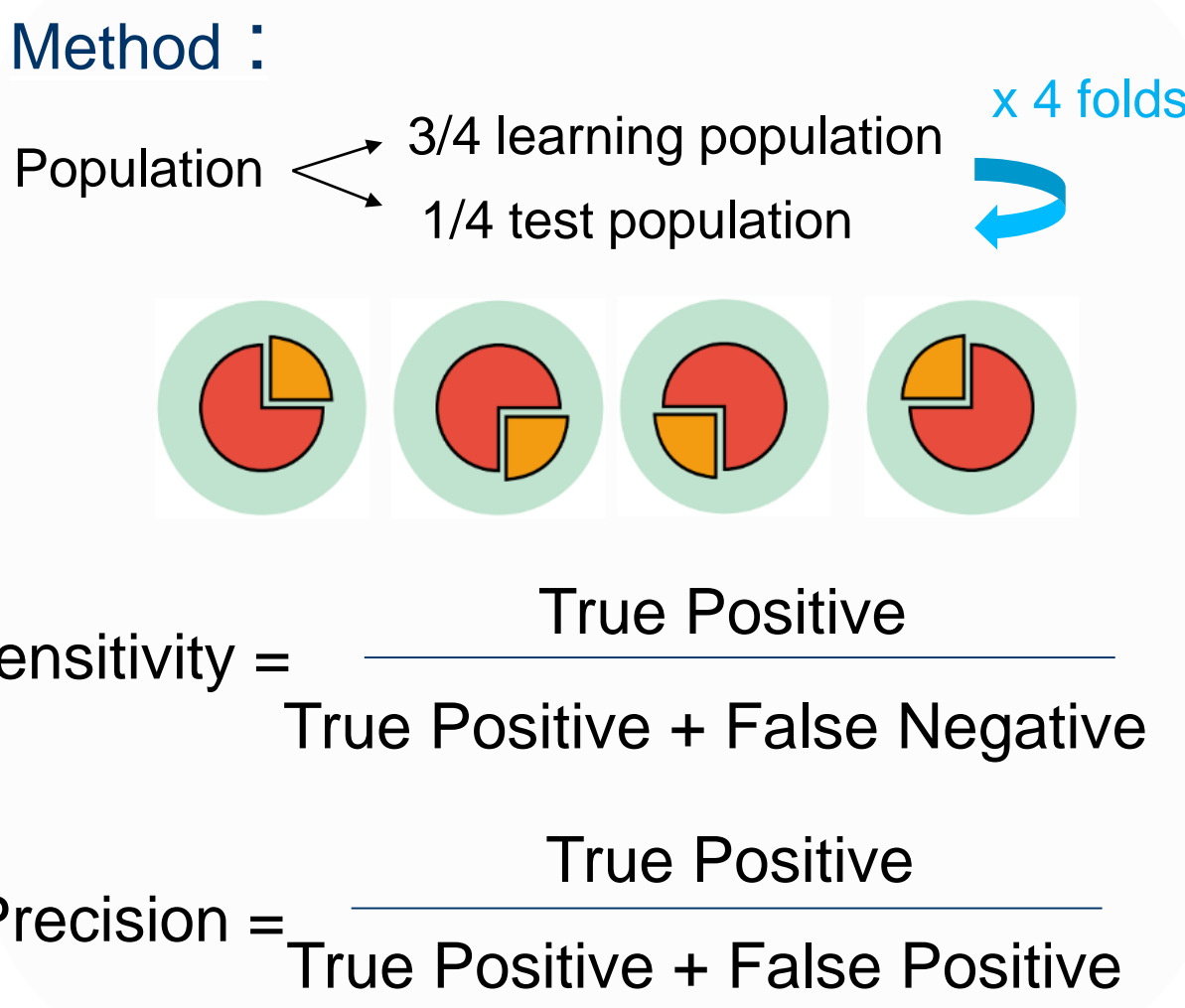
Global analysis and object classification of the entire image.
Access to unknown features (morphometric or others ?)
High number of features (~million)
Run time: few seconds / image

Results & Conclusions

Cross-validation

Evaluation on 4 different phenotypes
Nbr molecule / phenotype : Ph 1(X), Ph 2 (x), Ph 3(X) and Ph 4 (X)
Nbr images / phenotype : Ph 1(162), Ph 2 (180), Ph 3(297) and Ph 4 (414)

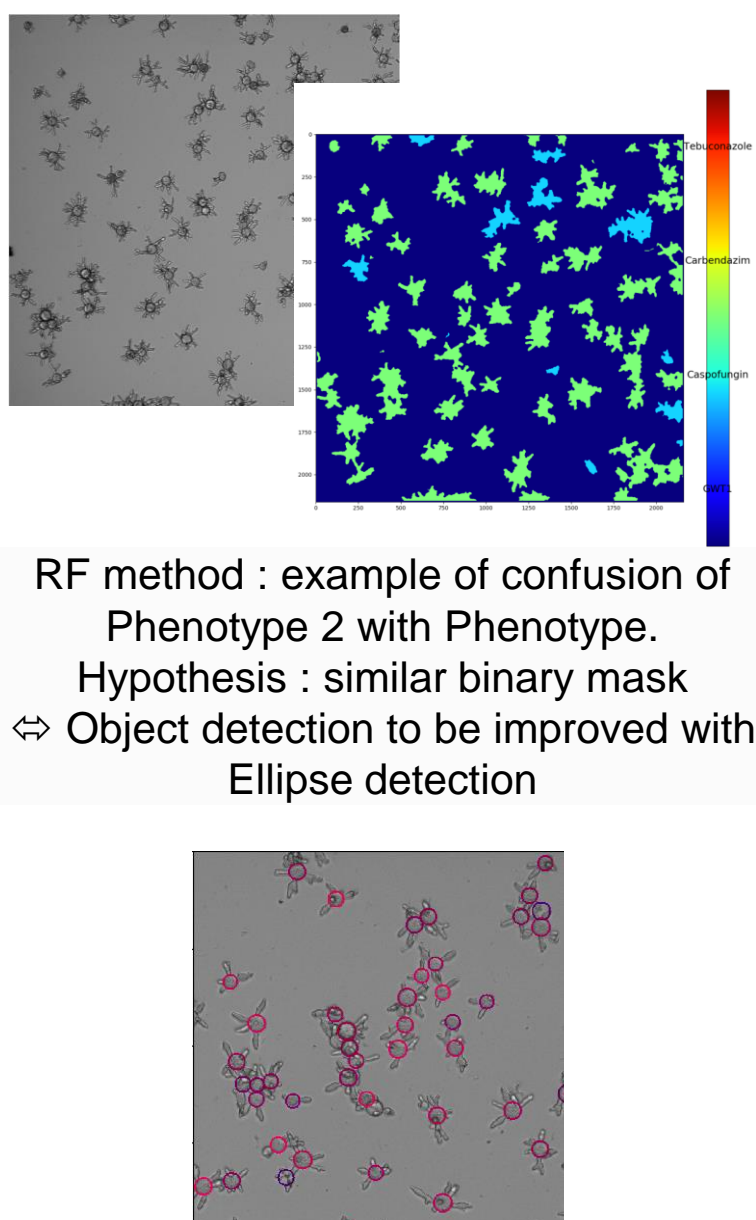
		Fold 1	Fold 2	Fold 3	Fold 4
RF n = 500 trees	Nbr of molecule with correct prediction	19 / 23	20 / 23	17 / 23	14 / 22
	Sensitivity (%)	77			
	Precision (%)	79			
CNN n = 500 training steps	Nbr of molecule with correct prediction	23 / 23	21 / 23	22 / 23	21 / 22
	Sensitivity (%)	92			
	Precision (%)	95			



Robustness intra-experiments

Evaluation on 4 different phenotypes, Nbr of images / experiments
E1 : Ph 1(99), Ph 2 (99), Ph 3 (189) and Ph 4 (243)
E2 : Ph 1(63), Ph 2 (81), Ph 3 (99) and Ph 4 (171)

		Training set E1, Test E2	Training set E2, Test E1
RF n = 500 trees	Nbr of molecule with right prediction	15 / 35	17 / 57
	Sensitivity (%)	37	
	Precision (%)	38	
CNN n = 500 training steps	Nbr of molecule with right prediction	31 / 35	54 / 57
	Sensitivity (%)	92	
	Precision (%)	91	



To date, CNN provides better phenotype classification than Random-Forest based method.
We are going to further investigate respective approaches in order to evaluate which one, or a combination, will permit to ensure a robust automation of phenotyping recognition in a larger number of phenotype.